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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,810	09/21/2006	Rosamund Carol Smith	X16397	2564

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EXAMINER	
SZPERKA, MICHAEL EDWARD	
ART UNIT	**PAPER NUMBER**
1644	

NOTIFICATION DATE	DELIVERY MODE
02/18/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patents@lilly.com

Office Action Summary	Application No.	Applicant(s)	
	10/593,810	SMITH ET AL.	
	Examiner	Art Unit	
	Michael Szperka	1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 June 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,7-9 and 14-17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,7-9 and 14-17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *9/21/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

1. Applicant's preliminary amendment received June 28, 2007 is acknowledged.

Claims 2-6 and 10-13 have been canceled.

Claims 7-9, 14, 16, and 17 have been amended.

Claims 1, 7-9, and 14-17 are pending in the instant application.

Information Disclosure Statement

2. The IDS form submitted 9/21/06 is acknowledged and has been considered. Citations AL and AM have been lined through since US provisional applications are not published documents that are freely available to the public and applicant has not provided a copy of these applications to be placed in the file wrapper of the instant application in conjunction with the filing of the 9/21/06 IDS.

Claim Rejections - 35 USC § 112

3. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claim 8 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Dependent claim 8 recites a humanized antibody of claim 1. Independent claim 1 recites antibodies "comprising" specific pairings of full length variable heavy and variable light chain domains. The specification discloses in Example 1 that these sequences were isolated from a Fab library made from a vaccinated C57Bl/6 mouse. Note that the full length variable domains comprise FR1-CDR1-FR2-CDR2-FR3-CDR3-FR4, and as such any claim dependent from the independent claim must minimally comprise the entirety of the recited SEQ ID numbers.

Queen et al. in US Patent 6,537,781, disclose a process for humanizing antibodies in which the non-human framework sequences of a variable domain are replaced with human sequences to minimize immunogenicity. Note that the comprising language of the independent claim does not allow for any alterations within the recited SEQ ID number sequences, and that said SEQ ID Numbers comprise murine framework sequences. Thus, a skilled artisan cannot make a humanized antibody that comprises an intact murine variable domain.

5. Claims 16 and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claims contain subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Applicant has claimed methods of treatment wherein antibodies comprising specifically recited antibody heavy and light chain variable domain pairings that bind myostatin/GDF-8 are administered to treat numerous diseases and disorders. The specific antibody variable domain sequences recited in independent claim 1 do not appear to have been disclosed in the prior art, but the prior art does indicate that administering antibodies that bind myostatin increases skeletal muscle mass and appears to be beneficial in diabetes treatments (US Patents 6,468,535 and 6,368,597 respectively, of record on the 9/21/06 IDS). Indeed, example 5 of the instant application indicates that administration of one of the antibodies of the instant invention caused mice to demonstrate increased skeletal muscle and bone mass as compared to animals which had been administered an irrelevant antibody.

However, the diseases, disorders, and conditions recited in the instant claims are quite broad and varied in their etiology and routine management. For example, the causes for liver disease and failure are numerous, including alcohol poisoning, hepatitis caused by infectious agents including viruses and bacteria, and fibrosis caused by injury and genetic defects that give rise to inborn errors of metabolism (Merck Manual, pages 368-386, see entire document). None of these conditions routinely utilize administration

of antibodies that bind myostatin, and it is not clear how increased skeletal muscle mass would help a person suffering congenital hepatic fibrosis due to an autosomal recessive malformation. Similarly, while the role for myostatin in inhibiting skeletal muscle growth is well documented, Cohn et al. studied the role of myostatin as a negative regulator of cardiac muscle using knockout mice and found that myostatin does not function as a major regulator of myofiber growth and regeneration in cardiac muscle in vivo (see entire document, particularly the right column of page 293). Thus, Cohn state that it is unclear what role, if any, myostatin plays in cardiac muscle (see particularly the top of the right column of page 295) and that thus their data would not predict any improvement in cardiac function of patients treated with myostatin inhibitors such as are now in clinical trials (see particularly the end of the last full paragraph of page 295). Thus, while myostatin inhibiting antibodies do increase skeletal muscle mass, they are not likely to increase cardiac muscle mass and claim 16 makes no discrimination among the different types of muscles found in mammalian organisms.

Therefore, based upon the breadth of the claims, the guidance and working examples of the specification, and the teachings of the art, a skilled artisan would be unable to practice the full breadth of the claimed invention without first conducting additional unpredictable research.

Double Patenting

6. The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

7. Claims 1, 7, 14, 16, and 17 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-26 of copending Application No. 12/066,664. Although the conflicting claims are not identical, they are not patentably distinct from each other because the antibody variable heavy and light chain sequences recited in the instant and copending claims are the same. Further, the specification of the copending application indicates that the antibodies of the copending application are to be used in practicing treatments methods such as those that have been recited in the instant claims. Additionally, the instant specification indicates that antibodies of the instant invention are not limited to the specific pairings of variable heavy and light domains recited in independent claim 1 as is evidenced by pages 4-5 of the instant specification.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims 8 and 15 are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-26 of copending Application No. 12/066,664 in view of US patent 5,530,101. The claims of the copending application have been discussed above and differ from the instant claimed invention in that they do not recite that the antibodies are humanized or comprise a carrier as part of a pharmaceutical composition. The '101 patent discloses that humanization provides the benefit of reduced antigeneicity for therapeutically administered antibodies, and provides numerous working examples wherein mouse monoclonal antibodies were humanized. The '101 patent further discloses that pharmaceutical compositions comprising humanized antibodies routinely comprise

carriers. Thus the differences between the copending claims and instant claims are minor modifications that are well known in the art and are obvious and routine to persons of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection.

9. Claim 9 is provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 22-26 of copending Application No. 12/066,664 in view of US patent 6,537,781. The claims of the copending application have been discussed above and differ from the instant claimed invention in that they do not recite that the antibodies comprise a non-human constant domain. The '781 patent discloses that antibodies which are to be used in methods of treating animals, such as dogs, may be "caninized" in the same way that therapeutic antibodies are humanized prior to administration to humans, the benefits of this including reduced antigeneicity of the therapeutically administered antibodies in the animal patient. Thus the differences between the copending claims and instant claims are minor modifications that are well known in the art and are obvious and routine to persons of ordinary skill in the art.

This is a provisional obviousness-type double patenting rejection.

10. No claims are allowable.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael Szperka whose telephone number is (571)272-2934. The examiner can normally be reached on M-F 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Eileen O'Hara can be reached on 571-272-0878. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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